be controlled with respect to donor-to-donor variability in disease severity and age, sufficient numbers of cells are not readily obtained from random operative procedures, and the phenotypic stability and proliferative capacity are lost upon serial subculture. Since the stability of the phenotype of isolated chondrocytes is critically dependent on cell shape and cell density, high-density micromass cultures are useful if sufficient numbers of chondrocytes are isolated. It is also possible to expand the cultures through a limited number of passages and re-differentiate the cells in fluid or gel suspension culture systems, where the chondrocytes regain morphology and the cessation of proliferation is associated with re-expression of cartilage phenotype. Culture systems that support chondrocyte phenotype include suspension culture in spinner flasks, in dishes coated with a non-adherent substrates, in pellets, and in 3-dimensional matrices such as collagen gels, agarose, alginate, or collagen sponges. Serum-free defined media of varying compositions, but usually including insulin, have also been used, frequently in combination with the other culture systems mentioned above. In explant cultures of articular cartilage, the chondrocytes remain encased within their own extracellular matrix and cellular function can be assessed by immunohistochemistry or in situ hybridization. Immortalized chondrocytes of human origin have been developed by several laboratories to serve as reproducible models for studying chondrocyte function. However, expansion of primary or immortalized chondrocytes in monolayer culture results in decreased expression of phenotypic markers, particularly if high cell density is not maintained. Suspension culture systems may be used to re-induce or maintain the expression of chondrocyte-specific markers. Retroviral transduction of SV40-TAg, HPV-16 E6/E7, or telomerase has been used somewhat successfully to immortalize primary human chondrocytes. However, the source and developmental state of the isolated chondrocytes, e.g. adult articular or juvenile costal, have influence on the retained characteristics such as proliferative capacity and differentiated phenotype. We have used immortalized human chondrocyte cell lines most successfully in studies requiring large numbers of cells, including assays of COL2A1 and MMP-13 promoter activities in luciferase reporters in response to cytokine treatments and overexpressed transcription factors, EMSA analysis using nuclear extracts, chromatin immunoprecipitations, and microarray analyses. Immortalized chondrocytes are not considered as substitutes for primary chondrocytes, in which definitive experiments should be repeated, but they serve as useful tools for evaluating and further validating mechanisms relevant to cartilage biology.

BIOMECHANICS OF OBESITY

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Obesity has a detrimental effect on biomechanical measures of function, including strength, balance, foot pressure, and gait. This workshop will review the related obesity literature, including the work of Hills, and DeVita as well as our own that will illustrate the tremendous burden obesity places on function. In addition, our work with obesity centers around its status as a major risk factor for knee osteoarthritis. Hence, this workshop will include the results of our work with obese adults with knee osteoarthritis. Obesity is well known as a major risk factor for type II diabetes and heart disease, however, less is known about its influence on strength and movement. This workshop will demonstrate how obesity negatively influences the way we move, resulting in orthopaedic problems and osteoarthritis. Finally, the positive effects of weight loss, either through diet and exercise or surgically induced will be discussed.

DOES SUBCHONDRAL BONE TISSUE REMODELING OR CELL FUNCTION PLAY A ROLE IN ARTICULAR CARTILAGE LOSS IN OSTEOARTHRITIS?

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Purpose: Osteoarthritis (OA) is the most common form of arthritis and accounts for billions in health and economical expenses in North America. OA is characterized by cartilage damage and loss, synovial membrane inflammation, bone sclerosis and the formation of osteophytes. Clinical and in vitro studies suggest that subchondral bone sclerosis and altered bone remodeling, due to abnormal osteoblasts (Ob), is involved in the progression and/or onset of OA. Several recent investigations have keyed in on the understanding of bone changes that may account for joint deterioration and development of OA. The hypothesis of a possible role for subchondral bone in the initiation and progression of cartilage degeneration speculates that the increase in bone mass and thickness could have modified the biomechanical properties of the tissue and could have favored the appearance/progression of articular cartilage structural changes.
Methods: Many studies have demonstrated that the subchondral bone is the site of several dynamic morphological changes that vary over time during the evolution of the disease and seem to be part of the disease process. Here we reviewed the evidence that OA Ob are responsible: i) to maintain this abnormal mineralization, ii) to release factors that can modify both osteoblasts and chondrocytes functions, and iii) to degrade articular cartilage.
Results: Individuals with OA exhibit striking increases in bone mass for affected sites, such as the knee and hip, as well as non-synovial sites, such as the lumbar spine. OA individuals also show increases in body mass index (BMI). This increase in bone mass is due to an abnormal metabolism of Ob as observed in vivo and in vitro, and most particularly in the subchondral bone tissue. These alterations of Ob from the subchondral bone tissue do not appear to be the consequence of a change in serum levels of humoral factors or hormones, but a response to altered local signals. OA Ob could show abnormal features due to paracrine/autocrine signals and indeed, OA Ob release abnormal levels of a number of growth factors, cytokines/chemokines and eicosanoids such as prostaglandins (PGs) that may all be involved both in abnormal Ob and chondrocytes cellular function. Growth factors such as Insulin-like growth factor-1 (IGF-1), Transforming growth factor-Î²1 (TGF-Î²1) and Hepatocyte growth factor (HGF) are all released more abundantly by OA Ob and have direct effects on Ob functions, osteophyte formation and cartilage catabolism. OA Ob release more Interleukin-6, CXCL12, CXCL13 and leptin that can also directly modulate type 1 collagen synthesis, promote articular cartilage degradation, and contribute to the inflammatory state observed in OA. Last, OA Ob release variable levels of PGE2, a situation that is related to both abnormal in vitro mineralization and altered cartilage catabolism. A number of key studies have indicated that conditioned-media from OA Ob alter chondrocyte cell functions and can degrade articular cartilage. However, we still do not know what this putative factor(s) is.
Conclusions: In conclusion, theses studies suggest that the mechanism(s) that lead to abnormal mineralization of OA bone tissue observed in vivo and those that lead to articular cartilage degradation may be linked with the release of a putative soluble factor(s) by OA Ob. Production of an abnormal collagen matrix and a soluble factor(s) by OA Ob leads to an abnormal osteoid matrix not mineralizing normally. This putative factor(s) contributes to cartilage degradation but also to abnormal Ob cell function.